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FALK, ANNE MARIE	
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1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/18/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	**Application No.** 10/677,301	**Applicant(s)** ONO ET AL.
	Examiner Anne-Marie Falk, Ph.D.	**Art Unit** 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *1-4 and 18-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/446,913.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

The amendment filed July 19, 2005 has been entered. Claims 5, 10, and 15 have been amended. The remarks filed April 20, 2005 (hereinafter referred to as "the response") are considered herein. Accordingly, Claims 1-23 remain pending in the instant application.

Claims 1-4 and 18-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. Applicant timely traversed the restriction requirement in the reply filed on September 27, 2004.

Accordingly, Claims 5-17 are examined herein.

Sequence Rules

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Sequences are disclosed in the specification and/or figures that are not identified by their sequence identifier (i.e., SEQ ID NO:). For example, there is a nucleotide sequence at page 12, line 5 that is not identified by its sequence identifier. Applicant is reminded that the entire specification and figures should be reviewed for sequence disclosures and that each sequence disclosed in the specification must be identified by its sequence identifier (i.e., SEQ ID NO:). The specification must be amended to identify all disclosed sequences by their sequence identifier (i.e., SEQ ID NO), in accordance with 37 CFR 1.821(d).

Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. 1.821(g). Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Claim Objections

Claim 9 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The limitation of Claim 9, "wherein said compound is a nucleic acid or a nucleic acid analog," is already present in Claim 5. Thus, Claim 9 fails to further limit the subject matter of Claim 5 from which it depends.

Double Patenting

Applicant is advised that should Claim 5 be found allowable, Claim 9 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). For the reasons detailed above, the scope of Claims 5 and 9 are identical.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 5-17 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 5, 6, 8, 9, and 12-23 of allowed U.S. Application No. 09/446,913. Although the conflicting claims are not identical, they are not patentably distinct from each other because the allowed claims are directed to treating a cerebral vasospasm associated with a subarachnoid hemorrhage by administration of a compound that inhibits the activation of a gene by NF-κB. The instant claims are more broadly directed to treating a brain disorder. Since a cerebral vasospasm would be considered a species of the broader genus of "brain disorders," the instant claims are anticipated by the allowed claims of U.S. Application No. 09/446,913. A species claim always anticipates a genus claim. Since the composition recited in the allowed claims would be considered a species of the broader genus of "a composition comprising a compound which inihibits the activation of a gene by NF-κB and which is a nucleic acid or nucleic acid analog which comprises a consensus sequence of the NF-κB binding site, and a carrier," which is the composition recited in the instant claims, the instant claims are anticipated by the allowed claims of U.S. Application No. 09/446,913. A species claim always anticipates a genus claim.

At page 5 of the reply filed July 19, 2005, Applicants state that they may amend the claims to overcome the rejection or file a terminal disclaimer. Applicants again request that this rejection be held in abeyance pending the identification of otherwise allowable subject matter.

Thus, the rejection is maintained for reasons of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-17 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants are referred to the guidelines on written description published January 5, 2001 in the Federal Register at Volume 66, Number 4, pp. 1099-1111 (also available at www.uspto.gov).

The claims are directed to the use of a composition comprising a compound which inhibits the activation of a gene by NF-κB, wherein the compound is a nucleic acid or nucleic acid analog which comprises a consensus sequence of the NF-κB binding site. However, use of the term "a consensus sequence" is indefinite for the reasons discussed hereinbelow. Furthermore, the instant specification does not describe "a consensus sequence of the NF-κB binding site." All claims recite an intended use, i.e. that the agent can be used to treat a brain disorder.

The specification does not provide a written description of any nucleic acid or nucleic acid analog that can be used for brain protection other than the rabbit sequence disclosed at page 12, line 5 (presumably SEQ ID NO: 1). In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, only SEQ ID NO: 1 is disclosed as an agent that acts as an NF-κB decoy and provides protection against particular types of brain damage when delivered using a cationic liposomal delivery system. SEQ ID NO: 1 is described as a rabbit NF-κB recognition sequence. The specification does not describe other targets for other species. Moreover, no other brain-protective agents of the type recited in the claims are described. Next then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics. In this case, the specification does not describe any other brain-protective nucleic acids by other relevant identifying characteristics.

A nucleic acid molecule is a complex chemical compound, and it is well-established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials. See *Oka* 7 USPQ2d at 1171. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinquish it. **It is not sufficient to define it solely by its principal biological property**, because an alleged conception having no more specificity than that **is simply a wish to know the identity of any material with that biological property**. *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).

This limited information is not deemed sufficient to reasonably convey to one skilled in the art that Applicants were in possession of the genus of NF-κB inhibitory nucleic acids with brain-treating activity, at the time the application was filed. Thus, it is concluded that the written description requirement is not satisfied for the claim-designated genus of NF-κB inhibitory nucleic acids that can be used in treating a brain disorder.

At page 6 of the response, Applicants assert that the specific NF kappa motif sequence GGGACTTTCC and the general consensus sequence GGGRNNYYCC were well-known in the prior art as shown by several references. Applicants cite Schreck et al. (1990), Zabel et al. (1991), Ranganathan et al. (1993), Xie et al. (1994), Lenardo et al. (1989), Grilli et al. (1993), Liou et al. (1993), and Siebenlist et al. (1994) as support for this assertion. The references have been fully considered. A complete review of the references reveals that a number of different specific sequences are disclosed. Moreover, a number of different sequences referred to as consensus sequences are disclosed in the references. Both Schreck et al.

and Zabel et al. disclose the GGGACTTTCC sequence. Ranganathan et al. disclose this sequence as well as the sequence GGGAATTTCC. Xie et al. disclose the generalized consensus sequence GGGRNNYYCC and 3 specific sequences (page 4705). Lenardo et al. disclose 10 specific sequences and a different generalized consensus sequence (Table 1, last item). Grilli et al. disclose the sequence GGGACTTTCC (page 19). Liou et al. disclose 8 different specific sequences (Table 5), some of which do not meet the requirements of the generalized consensus sequence of Xie et al. (i.e., GGGRNNYYCC). Siebenlist et al. disclose the generalized consensus sequence GGGRNNYYCC (page 407, paragraph 1).

U.S. Patent No. 6,410,516 (Baltimore et al., filed June 5, 1995) discloses yet another generalized consensus sequence (Table 2, last item). Thus, Xie et al., Lenardo et al., and Baltimore et al. each disclose a different generalized consensus sequence.

Lewin (1990) discloses that the consensus sequence for the κB motif is GGGACTTTCC (page 555, Table 29.4). Thus, at least four different sequences in the prior art are referred to as consensus sequences.

All 8 references, as well as the Baltimore et al. patent, disclose the sequence GGGACTTTCC (Siebenlist et al. disclose it at page 413.

Xie et al. acknowledges that the generalized sequence GGGRNNYYCC represents 128 possible specific sequences, only 20 of which have been reported in nature (page 4705, column 2, paragraph 2). Xie et al also teaches that GGGACTTCC is the most common sequence among the 20 that have been found (page 4705, column 2, paragraph 2).

Of the 128 possible specific sequences represented by the generalized consensus sequence GGGRNNYYCC, with the possible exception of GGGACTTCC, any given one would **not** be considered a consensus sequence. Nevertheless, the **claims** require the administration of a **consensus** sequence. Applicants seem to be arguing that any one of the 128 sequences represented by the generalized consensus sequence GGGRNNYYCC **is** itself a consensus sequence and thus meets the claim limitation, which recites administration of "a consensus sequence." This is clearly **not** the case. There are not 128 **consensus** sequences. Furthermore, one of skill in the art clearly cannot **administer** the generalized consensus sequence GGGRNNYYCC, because this notation is merely a representational result from the analysis of multiple specific sequences found in nature.

A consensus sequence is a defined sequence, either generalized or specific, that results from analysis of a given multiple sequence alignment. Different multiple sequence alignments may result in different consensus sequences. In other words, including or excluding a sequence from a multiple sequence alignment can change the consensus sequence that results from analysis of those different data sets. The references discussed above aptly demonstrate that different data sets give different results. Thus, the "consensus" sequence may change over time as new sequences become available.

Lewin (1990) defines "**consensus sequence**" as "an idealized sequence in which each position represents the base most often found when many actual sequences are compared" (page 808). Given this definition, any given sequence alignment should give only a single consensus sequence, either generalized or specific. As discussed above, however, different sequence alignments can give different resultant consensus sequences.

Thus, there are discrepancies in the prior art as to what can be considered "a consensus sequence of the NF-κB binding site," as recited in the claims. Given the discrepancy, it is the function of the instant specification to provide a written description of the element to clearly convey the intended meaning and the scope of the claim terminology. Nevertheless, there is no question regarding the generalized consensus sequences disclosed in the prior art; a generalized sequence cannot be administered to a subject, for the reasons discussed above. Furthermore, given the disclosures of the prior art, SEQ ID NO: 1 of the instant application clearly is not a consensus sequence.

Claim 15 recites "the consensus sequence of the NF-κB binding site." Use of the definite article "the" denotes a single particular consensus sequence, but the instant specification does not provide a written description of "the consensus sequence of the NF-κB binding site" any more than it describes "a consensus sequence." The specification only describes SEQ ID NO: 1 which does not appear to be "the consensus sequence" or even "a consensus sequence" given the teachings of the prior art.

Thus, contrary to Applicants' argument, there is no written description of "**a** consensus sequence" or "**the** consensus sequence," as claimed. Therefore, the written description rejection is maintained.

Claims 5-17 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of an NF-κB inhibitory nucleic acid comprising SEQ ID NO: 1 and a liposomal delivery system, wherein the inhibitor diminishes cerebral vasospasm associated with subarachnoid hemorrhage, does not reasonably provide enablement for the use of any NF-κB inhibitory nucleic acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claimed invention is directed to administration of an NF-κB inhibitory nucleic acid for treatment of a brain disorder. The specification discloses the administration of a double-stranded oligonucleotide (SEQ ID NO: 1) using a cationic liposomal delivery system. The only use taught in the specification for the claimed compositions is for producing a therapeutic effect, specifically brain protection. Thus, the invention is directed to administering a nucleic acid molecule for therapy. Therefore, the only use for the claimed compositions is for gene therapy. The claims are very broad with regard to the intended patients and disorders that can be treated. The claims encompass an intended use for treating any type of brain disorder. When an intended use is recited, the claimed method must be enabled over the full scope for the intended use. The specification contemplates a wide variety of brain disorders that allegedly could be treated using the claimed compositions (see page 3, paragraph 3 to page 4, paragraph 1). However, the specification does not teach how to use the claimed methods over the full scope to achieve a therapeutic effect, for the following reasons.

Gene therapy is not routinely successful. Therefore, the disclosure must teach how to use the claimed method for the intended use, over the full scope. At the time the application was filed, the art of administering any type of genetic expression vector to an individual so as to provide a tangible therapeutic benefit was poorly developed and unpredictable. The NIH ad hoc committee to assess the current status and promise of gene therapy reported in December 1995 that "clinical efficacy has not been definitively demonstrated at this time in any gene therapy protocol, despite anecdotal claims...," and that "significant problems remain in all basic aspects of gene therapy" (Orkin and Motulsky, p. 1). In a review article published in Scientific American in June 1997, Theodore Friedmann discusses the technical barriers which have so far prevented successful gene therapy, and states "So far, however, no approach has definitively improved the health of a single one of the more than 2,000 patients who have enrolled in gene therapy trials worldwide" (p. 96). In a review article published in Nature in September 1997, Inder Verma states "Although more than 200 clinical trials are currently underway worldwide, with hundreds of patients enrolled, there is still no single outcome that we can point to as a success story" (p. 239). The instant specification does not adequately teach one skilled in the art how to use the claimed methods for *in vivo* gene therapy. Thus, absent any showing that the claimed methods can be used in gene therapy applications to produce the intended therapeutic effect in an immunocompetent animal, such as a human, the claims directed to gene therapy are not enabled by the disclosure.

The specification fails to provide an enabling disclosure for targeting appropriate cells for the treatment of the diseases referred to in the specification. The specification contemplates treating a wide variety of diseases and disorders using the claimed method, including cerebral vasospasm following subarachnoid hemorrhage, cerebral infarcts in cerebral thrombosis and cerebral embolism, sequelae of intracranial hemorrhage, cerebrovascular dementia, hydrocephalus, cerebral arterial anomaly-angioma, various brain tumors, Parkinson's syndrome, cerebral arteriosclerosis, meningitis, encephalitis, AIDS, various types of encephalopathy, multiple sclerosis, and brain disorders arising from neuronal death caused by serious head trauma (see pages 3-4). Only general guidance is offered with regard to delivering the agent to the appropriate site. However, the art recognizes that targeting strategies are not currently sufficient to overcome the problems known in the art. More importantly, the disclosure does not offer a solution to this problem. While progress has been made in recent years for *in vivo* gene transfer, vector targeting to desired tissues *in vivo* continues to be unpredictable and inefficient as supported by numerous teachings in the art. For example, Miller et al. (1995) review the types of vectors available for *in vivo* gene therapy, and conclude that "for long-term success as well as the widespread applicability of human gene therapy, there will have to be advances ... targeting strategies outlined in this review, which are currently only at the experimental level, will have to be translated into components of safe and highly efficient delivery systems" (page 198, column 1). Deonarain et al. (1998) indicate that one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time" (page 53, first paragraph). Deonarain et al. review new techniques under experimentation in the art which show promise but states that such techniques are even less efficient than viral gene delivery (see page 65, first paragraph under Conclusion section). Verma et al. (1997) review vectors known in the art for use in gene therapy and discuss problems associated with each type of vector. The teachings of Verma et al. indicate that a resolution to vector targeting has not been achieved in the art (see entire article). Verma et al. also teach that appropriate regulatory elements may improve expression, but that it is unpredictable which tissues such regulatory elements target (page 240, sentence bridging columns 2 and 3). Crystal et al. (1995) also review various vectors known in the art and indicate that "among the design hurdles for all vectors are the need to increase the efficiency of gene transfer, to increase target specificity and to enable the transferred gene to be regulated" (page 409).

In view of the quantity of experimentation necessary to determine appropriate parameters for using the claimed method to achieve a therapeutic effect, and given the lack of applicable working examples demonstrating an *in vivo* effect for brain disorders other than cerebral vasospasm associated with subarachnoid hemorrhage, the limited guidance in the specification, particularly with regard to the nucleic acid that is to be delivered, the broad scope of the claims, and the unpredictability for using the claimed method in treating the wide variety of disorders set forth in the specification, undue experimentation would have been required for one skilled in the art to practice the claimed methods over the full scope.

At page 7 of the response, Applicants assert that one of skill in the art would know how to target an NF-κB decoy to the brain. Applicants cite the specification at pages 10-12. The cited section describes injecting the oligonucleotide into the cistern (subarachnoid administration). No other guidance is provided. There is no guidance regarding how one of skill in the art would therapeutically administer the decoy oligonucleotide to treat any other disease of the brain. The target site for NF-κB is in the nucleus of the cell. The inactive form of NF-κB is located in the cytosol and, once activated, the factor enters the nucleus. The activated form binds to its target site on double-stranded DNA. Therefore, the decoy must enter the cell, and the nucleus of the cell. Furthermore, the decoy oligonucleotide must enter the appropriate cell type in sufficient quantity to effectively compete against the endogenous target sites in the genome. Thus, the *in vivo* binding affinity of the decoy oligonucleotide for the protein and the amount of decoy actually delivered to the nucleus of the cell must be sufficient to effectively compete with the endogenous target site. Even if one of skill in the art knew where to inject the decoy into the brain for treatment of the very broad scope of diseases covered by the claims, which the skilled artisan does not, knowing where to inject the drug in no way addresses the problem of delivering the drug to the nucleus of the cell in sufficient quantities to produce a therapeutic effect, across the scope of all brain diseases.

At pages 7-8 of the response, Applicants assert that the specification discloses at page 3, last paragraph, that NF-κB decoys are particularly effective for use in brain tissues against disorders caused by unwanted activation of genes regulated by the NF-κB transcription factor. Applicants further assert that the top of page 4 describes a number of such diseases. Applicants cite several references to show the role of NF-κB in particular brain diseases, particularly Alzheimer's disease, cerebral infarction, HIV-1 encephalitis, head trauma, and convulsant-induced seizures. The references generally show increased NF-κB activity in subjects having these diseases or conditions. There is no evidence to show that decreasing NF-κB activity in these diseases would be therapeutic. An association does not necessarily indicate causation. Furthermore, there is no evidence that one of skill in the art could use the claimed method to effectively inhibit NF-κB-mediated gene activation to the extent necessary to produce a therapeutic effect. The response does not address the unpredictability in the gene therapy art. The rejection adequately demonstrates that the state of the art is such that even when intensive effort is applied to develop gene therapy protocols, success has been extremely limited. Thus, it is not enough to identify diseases where NF-κB may play a role in the pathological process because the rejection is based on the unpredictability in the gene therapy art, the limited guidance of the specification, the quantity of experimentation necessary to determine appropriate parameters for using the claimed method to achieve a therapeutic effect over the very broad scope of diseases, the lack of applicable working examples demonstrating an *in vivo* effect for brain disorders other than cerebral vasospasm associated with subarachnoid hemorrhage, and the broad scope of the claims with regard to the wide variety of diseases to be treated, the nucleic acid to be delivered, and the route of administration.

Given these considerations, undue experimentation would have been required for one skilled in the art to practice the claimed methods over the full scope. Therefore, the scope of enablement rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 15 stands rejected and Claims 5-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 remains indefinite in its recitation of "several units of a double-stranded nucleic acid or nucleic acid analog" because it is unclear what it is that is being referred to as a "unit."

At page 8 of the response, Applicants assert that this rejection is moot in view of the amendment. However, no amendment has been made to address this rejection. The claim continues to recite "several units of a double-stranded nucleic acid or nucleic acid analog." Applicants further assert that the term "unit" is described in the specification on page 5, lines 10-11 and that the term refers to a sequence comprising one or more repeats of a particular oligonucleotide sequence, such as tandem repeats of SEQ ID NO: 1. The sentence that Applicants refer to in the specification reads "[t]he still more preferred NF-kB decoy is a double-stranded oligonucleotide containing one or several units of said nucleotide sequence or a mutant thereof. Thus, although the term is used in the specification, the specification does not define the meaning of the term in the context in which it is used. There is nothing in the specification to apprise one of skill in the art of what would be considered a "unit."

Claims 5-17 are indefinite in their recitation of "a consensus sequence of the NF-kB binding site" (in Claim 5) because use of the indefinite article "a" denotes that numerous consensus sequences could be used. However, for the reasons discussed above under the written description rejection, given the art-recognized definition for "consensus sequence," the term denotes only a single sequence, not multiple sequences. Furthermore, the metes and bounds are not clearly set forth. This is a new rejection necessitated by the amendment to Claim 5.

Claims 11 and 14 are indefinite in their recitation of "comprises the base sequence of SEQ ID NO: 1" and "comprising the base sequence of SEQ ID NO: 1" because Claim 5 is limited to the use of "a consensus sequence," but SEQ ID NO: 1 is not a consensus sequence. Although generalized consensus sequences are taught in the prior art, Lewin (1990) teaches that a consensus sequence is an idealized sequence and that the consensus sequence for the κB motif is GGGACTTTCC Thus, the two different limitations are in conflict with each other. This is a new ground of rejection necessitated by the amendment to Claim 5.

Prior Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. U.S. Patent No. 6,262,033 (Morishita et al.) discloses the administration of an NF-κB decoy for the treatment of NF-κB-associated diseases. See especially Claim 1.

Conclusion

No claims are allowable.

This application contains claims 1-4 and 18-23 drawn to an invention nonelected with traverse in the reply filed September 27, 2004. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on (571) 272-4517. The central official fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER

Notice to Comply	Application No. 10/677,301	Applicant(s) Shigeki et al.	
	Examiner Anne-Marie Falk, Ph.D.	Art Unit 1632	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: Sequences listed in the specification and drawings must be identified by their sequence identifier.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the specification**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:
For Rules Interpretation, call (571) 272-2510
For CRF Submission Help, call (571) 272-2501/2583.
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